

U.S. SERIAL NO. 08/398,555  
FILED MARCH 3, 1995  
AMENDMENT AND RESPONSE TO ADVISORY ACTION

### In the Claims

1. (twice amended) A composition for stimulating the growth of eukaryotic cells comprising

a biocompatible solid substrate,

biocompatible synthetic branched water soluble polymeric tethers, and

growth effector molecules,

wherein one end of each tether is covalently linked to the substrate and each growth effector molecule is covalently linked to a distal end of a tether so that the growth effector

molecule cannot be internalized by cells attached to the substrate, each tether is able to bind <sup>covalently link</sup> ~~more than one growth effector molecule~~, and

the growth effector molecules are attached to the substrate in a concentration effective to enhance the rate of target cell growth over the rate of target cell growth with soluble growth effector molecules and growth effector molecules adsorbed to a substrate without internalization of the molecules.

5. (twice amended) The composition of claim 4 wherein the substrate polymer is selected from the group consisting of synthetic polymers and natural polymers.

6. (twice amended) The composition of claim 5 wherein the substrate polymer is selected from the group consisting of proteins, polysaccharides, [extracellular matrix proteins, ]polyesters, polycaprolactone, polyhydroxybutyrate, polyanhydrides, polyphosphazenes, polyorthoesters, polyurethanes, and combinations thereof.

Please cancel claim 7.

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8. (amended) The composition of claim 1 [7] wherein the tether is selected from the group consisting of polyethylene oxide[, ] and carboxymethylcellulose[, and starch].

13. (twice amended) A method for growing eukaryotic cells comprising

(a) bringing into contact the cells and a composition comprising

a biocompatible solid substrate,

biocompatible branched water soluble polymeric tethers, and

growth effector molecules,

wherein one end of each tether is covalently linked to the substrate,

each tether is able to bind more than one growth effector molecule, [and]

each growth effector molecule is covalently linked to a distal end of a tether so that the growth effector molecule cannot be internalized by cells attached to the substrate, and

the growth effector molecules are attached to the substrate in a concentration effective to enhance the rate of target cell growth over the rate of target cell growth with soluble growth effector molecules and growth effector molecules adsorbed to a substrate, without internalization of the molecules; and

(b) maintaining the contacting cells and composition under conditions and for a time sufficient to cause the cells to grow.

21. (amended) The method of claim 20 wherein the substrate polymer is selected from the group consisting of synthetic polymers and natural polymers.

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22. (amended) The method of claim 21 wherein the substrate polymer is selected from the group consisting of polylactic acid, polyglycolic acid, polyanhydrides, polyorthoesters, collagen, glycosaminoglycans, polyamino acids, and combinations thereof.

Please cancel claim 23.

24. (amended) The method of claim 13 [23] wherein the tether is selected from the group consisting of polyethylene oxide, carboxymethylcellulose, and starch.

31. (twice amended) A cell culture comprising  
a biocompatible solid substrate,  
biocompatible branched water soluble polymeric tethers,  
growth effector molecules, and  
growing cells,

wherein one end of each tether is covalently linked to the substrate, each tether is able to bind more than one growth effector molecule, [and]

each growth effector molecule is covalently linked to a distal end of a tether so that the growth effector molecule cannot be internalized by cells attached to the substrate, [and]

the growth effector molecules are attached to the substrate in a concentration effective to enhance the rate of target cell growth over the rate of target cell growth with soluble growth effector molecules and growth effector molecules adsorbed to a substrate, without internalization of the molecules, and wherein the growing cells are bound to the growth effector molecules.

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32. (twice amended) A method of testing a compound for an effect on tissue comprising

(a) bringing into contact the compound to be tested and a composition comprising  
a biocompatible solid substrate,  
biocompatible branched water soluble polymeric tethers,  
growth effector molecules, and  
growing cells,

wherein one end of each tether is covalently linked to the substrate,  
each tether is able to bind more than one growth effector molecule, [and]  
each growth effector molecule is covalently linked to a distal end of a  
tether so that the growth effector molecule cannot be internalized by cells  
attached to the substrate, [and]

the growth effector molecules are attached to the substrate in a  
concentration effective to enhance the rate of target cell growth over the rate  
of target cell growth with soluble growth effector molecules and growth  
effector molecules adsorbed to a substrate, without internalization of the  
molecules, and wherein the growing cells are bound to the growth effector  
molecules;

(b) incubating the compound and the composition under conditions promoting cell  
growth; and